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On December 8, 2005

TOWNSEND and TOWNSEND and CREW LLP

By: Lois M. Simón

AMENDMENT UNDER 37 CFR 1.116 EXPEDITED PROCEDURE – EXAMINING GROUP 1641

PATENT
Docket No.: 014058-013300US
Client Ref. No.: 208

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Sally Mossman
Lawrence S. Evans
Jory R. Baldridge

Application No.: 10/068,171

Filed: February 4, 2002

For: IMMUNOSTIMULANT COMPOSITIONS COMPRISING AMINOALKYL GLUCOSAMINIDE PHOSPHATES AND SAPONINS

Examiner: Wang, Shengjun

Art Unit: 1617

DECLARATION UNDER 37 C.F.R. 1.132 OF SALLY MOSSMAN

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SALLY MOSSMAN DECLARES AND STATES:

1. I received the degree of Pd.D. from The University of Liverpool, United Kingdom in 1990. I currently hold the position of Senior Scientist at Corixa Corporation, Seattle Washington, and am one of the inventors in this Application.

2. I understand that one requirement made by the examiner is to authenticate and to comment on the data in the examples contained in this patent application. Accordingly, I hereby state that all eight examples in this patent application were carried out in fact, and were conducted either by me or under my supervision.

3. I also understand that even with the data in these examples authenticated, the examiner still considers it an insufficient showing to establish unexpected results for the claimed combinations of alkyl glucosaminide phosphates (AGPs) and saponins. I note that at this time only a small class of alkyl glucosaminide phosphates are claimed, and I wish to state that I consider the data in the examples in this patent application, which focuses on two AGPs, nos. B3 and B19, to be sufficiently representative of the claimed class of AGPS so as to provide the necessary overall showing that combinations of the claimed AGPs with the claimed saponins produce unexpected results.

4. In particular, Tables 1 and 2 in Example 1 show that combinations of the AGPs B3 and B19 with the saponin Quil-A produce surprising and unexpected results, especially with respect to specific lysis, than the saponin alone, and as compared with the emulsion vehicle alone. In Table 2, for instance, the vehicle alone produced 4-5% lysis; that value rose to 13-35% when Quil A was added; and when the AGPs were added with the saponin the values were primarily 50+ percent. These results, to me, are unexpected from the performance of either the vehicle alone or the saponin alone.

5. The following additional experiments were conducted, either by me or under my supervision, using combinations of the saponin QS-21 and three AGP compounds, designated RC-527, RC-540 and RC-557.

6. AGP compound RC-527 is an AGP within the definition of current claim 91 in which R^1, R^2 and R^3 are each n-$C_9H_{19}CO$, R^4 and R^5 are both hydrogen, *n* and *p* are both zero, and R^6 is COOH.

7. AGP compound RC-540 is an AGP within the definition of current claim 91 in which R^1, R^2 and R^3 are each n-$C_9H_{19}CO$, R^4 and R^5 are both hydrogen, *n* is 1, *p* is 1, and R^6 is OH.

8. AGP compound RC-557 is an AGP within the definition of current claim 91 in which R^1, R^2 and R^3 are each n-$C_{13}H_{27}CO$, R^4 and R^5 are both hydrogen, *n* is 2, *p* is zero, and R^6 is hydrogen.

9. This example demonstrates the synergy between a saponin adjuvant when combined with an AGP adjuvant, such that greater levels of CTL activity and interferon-gamma secretion are induced with the combination than by either adjuvant alone, or in the absence of adjuvant. This experiment employed a recombinant polypeptide antigen from M. tuberculosis, referred to as rDPV (rMtb 8.4) (Coler *et al.* (1998) *J. Immunol.* 161:2356-2364) to immunize C57BL/6 mice subcutaneously. Briefly, groups of four female 6-8 week old C57BL/6 mice were immunized subcutaneously with 5μg rDPV combined with 10 μg of the AGP compounds RC-527, RC-529 (compound B19 in this patent application), RC-540 and RC-557 as well as several other AGPs, 10 μg QS-21 or a combination of QS-21 and an AGP adjuvant, formulated in both aqueous (AF) and oil emulsion (SE) formulations. The AGP aqueous formulations comprised DPPC surfactant, in which the DPPC:AGP molar ratio was about 8:1. Additional mice received the equivalent dose of antigen formulated in adjuvant combinations comprising 3-O-deacylated monophosphoryl Lipid A (MPL®; Corixa Corp., Seattle, WA) and QS-21 in aqueous and oil emulsion formulations. A separate group of mice were immunized with 100 μg of pVR-1012/DPV (DPV DNA). Control mice were immunized with saline. Immunizations were performed at weeks 0, 3 and 7, and spleens were harvested 2 weeks later. Single cell suspensions of splenocytes were stimulated in vitro with EL-4 cells stably transduced to express DPV. Thirteen days later these cells were assayed for CTL activity against EL-4-DPV by standard chromium release techniques. Additional fresh splenocytes were stimulated in vitro with 5 μg/ml rDPV and supernatants were harvested 3 days later and assayed for IFN-γ by ELISA. The results of the above experiments are shown in the attached Figure 1 (for RC-527) and Figure 2 (for RC-540 and 557).

The Mean Specific Lysis (chromium release) is expressed as the mean of four mouse spleens per group, with background lysis against EL-4 cells subtracted, at an effector to target ratio ("E:T Ratio") of 12.5:1, 25:1, 50:1, and 100:1 (Figure 1).

9. Again, in my opinion, the data shows unexpected results for adjuvant combinations of QS-21 with RC-527, RC-540 and RC-557. The reason for my conclusion that the results of the tests of these three AGP compounds in combination with QS-21 saponin, described above, is unexpected, is that the adjuvant combinations induce an immune response that is greater in magnitude than that induced by either adjuvant alone.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the patent to which this verified states is directed.

11/18/05

SALLY MOSSMAN

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